RESEARCH POSTER PRESENTATIONS - SESSION IV

DISEASE- SPECIFIC STUDIES
CANCER – Clinical Outcomes Studies

PCN1
BONE SAFETY PROFILE OF DENOSUMAB THERAPY: A PHARMACOVIGILANCE CHARACTERIZATION ANALYSIS
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OBJECTIVES: Denosumab is a biologic approved in June 2010 to treat bone tumors and hypercalcemia of malignancy. This study characterizes bone-related safety signals of subtrochanteric atypical femoral fractures (SAF) and osteonecrosis of the jaw (ONJ) in relation to denosumab therapy. **METHODS:** The FDA Adverse Event Reporting System was used to detect signals of SAF and ONJ in relation to denosumab therapy. Adverse event reports submitted between July 2010 and December 2013 were retrieved and disproportional reporting of SAF and ONJ was calculated by Empirical Bayes Geometric Mean (EBGM). Denosumab-event pairs with EBGM 95% confidence interval lower limit ≥2.0 are considered signals of SAF and ONJ excess reporting compared to other drugs in the database. Events were defined by the Preferred Terms of the Medical Dictionary for Regulatory Activities, and denosumab was defined by the Anatomical Chemical Therapeutic Classification. **RESULTS:** A total of 26,216 adverse event reports submitted for denosumab during the analysis period, corresponding to 30 for SAF and 721 for ONJ. Denosumab was significantly associated with more than expected reporting of SAF (EBGM=17.5, 95%CI=9.67-30.0) and ONJ (EBGM=26.9, 95%CI=20.1-35.9) compared to other drugs. The majority of denosumab users who experienced both events were females, and average age was 69 years (SAF SD=9.5; ONJ SD=11.3). 12 SAF and 65 ONJ events lead to hospitalization; 25 and 14 ONJ events contributed to patient disability and death, respectively. Other factors could have lead to these serious outcomes, including comedications and comorbidities. **CONCLUSIONS:** SAF and ONJ are potential risks of denosumab therapy. Patients with thigh or hip pain should seek immediate medical help, and periodic dental and maxillofacial evaluations should be performed before and during denosumab therapy. Pharmacoepidemiologic studies are recommended to further characterize these risks, as some patients were treated with other medications, including systemic corticosteroids at the time of event occurrence.

PCN2
META-ANALYSIS OF THE SAFETY OF SIPULEUCEL-T IMMUNOTHERAPY IN PROSTATE CANCER
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OBJECTIVES: Sipuleucel-T is an autologous active cellular immunotherapy designed to reduce the risk of death in patients with prostate cancer. The aim of this study was to evaluate the safety of Sipuleucel-T for patients with prostate cancer. **METHODS:** PubMed, EMBASE and the Cochrane Central Register of Controlled Trials were searched through January 10, 2015. Criteria for inclusion were randomized, placebo-controlled clinical trials on Sipuleucel-T, patients receiving three infusions, 36 months follow-up and the availability of outcomes data for adverse events. The primary outcome was the total number of adverse events. Secondary outcomes examined eighteen specified adverse events. Two investigators selected studies independently and assessed the quality of studies using the Jadad scale. Point estimates with a 95% confidence interval were generated. Fixed-effects or random random-effects models were based on the evaluation of heterogeneity. **RESULTS:** Five clinical trials encompassing 1031 patients were included. The overall adverse events relative risk (RR) was 1.02 (95% CI 1.00 to 1.05, p=0.091). For the secondary outcomes, differences were detected between Sipuleucel-T and placebo on chills (RR 4.87; 95% CI 2.50 to 6.78, p=0.000; 904 patients), fatigue (RR 1.20; 95% CI 1.01 to 1.43, p=0.035; 1031 patients), pyrexia (RR 5.40; 95% CI 1.90 to 15.35, p=0.002; 1031 patients), headache (RR 2.68; 95% CI 1.75 to 4.10, p=0.000; 1031 patients), influenza like illness (RR 3.07; 95% CI 1.48 to 6.36, p=0.003; 681 patients), myalgia (RR 2.24; 95% CI 1.26 to 4.00, p=0.006; 681 patients), nausea (RR 1.40; 95% CI 1.05 to 1.88, p=0.023; 1031 patients), vomiting (RR 1.86; 95% CI 1.21 to 2.88, p=0.005; 856 patients) and dyspnea (RR 3.72; 95% CI 1.34 to 10.36, p=0.012; 350 patients). **CONCLUSIONS:** Sipuleucel-T significantly increased the risk of selected adverse events in patients with prostate cancer. Although many adverse events were transient, patients and providers should consider the potential risk of treatment with Sipuleucel-T.

PCN3
TREATMENT FOR CHEMOTHERAPY-RELATED COGNITIVE DYSFUNCTION: REVIEW OF THE LITERATURE
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OBJECTIVES: Chemotherapy-related cognitive dysfunction (CRCD), colloquially known as 'chemo fog' or 'chemo brain,' describes the impact of chemotherapy on cognitive functioning in domains ranging from memory to expressive language. CRCD is generally attributed to the direct or indirect effects of chemotherapy on the central nervous system, may occur at some level of intensity in as many as 75% of patients who have undergone chemotherapy, and impacts patient quality of life, educational/occupational achievement, and social functioning. Management of CRCD includes both pharmacological and non-pharmacological therapies. **METHODS:** To better understand the range of treatments that have been studied for CRCD, and their relative efficacy, a comprehensive review of the published literature was undertaken. A MEDLINE search was conducted for relevant sources published in English between January 2005 and December 2014. The search was limited to studies describing trials of interventions to manage or treat CRCD using non-pharmacological interventions. **RESULTS:** Of 161 records retrieved, 11 described interventions targeting CRCD. Pharmacological therapies used included erythropoietin, dexmethylphenidate, ginkgo biloba, and pycnogenol. Half of the studies focused on breast cancer. Most resulted in statistically non-significant findings, but two studies of erythpoietin and the pycnogenol trial had significant results. All 3 of the non-pharmacological studies focused on patients with breast cancer, two using a form of cognitive-behavior therapy (CBT) and the third studying a yoga program. **CONCLUSIONS:** The review found a large number of studies documenting the problem of CRCD, discussing innovative ways of measuring the extent of the cognitive impairment, and describing etiological theories, such as the relationship of CRCD to fatigue and anemia. However, there was a paucity of well-designed, sufficiently powered studies of potential treatments, given the extent of the problem and its impact on patient functioning. This is an area of clear patient need which warrants further scientific study.

PCN4
HYPOFRACTIONED RADIOTHERAPY IN THE TREATMENT OF EARLY BREAST CANCER: SYSTEMATIC REVIEW AND META-ANALYSIS
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OBJECTIVES: To evaluate short and long term effects of hypofractioned radiation therapy in women with early stage breast cancer, after undergoing breast conservative surgery. **METHODS:** We searched for randomized controlled trials in Embase, Medline, Cochrane Library and Lilacs comparing unconventional versus conventional fractioning. The authors performed data extraction independently. Disagreements were resolved by consensus. Random-effects risk ratios (RR) were calculated comparing patients randomized to unconventional with those to conventional fractioning. Periods before and after five years of treatment were considered. **RESULTS:** Five trials reported on 7.802 women. The studies were of medium to high quality. Unconventional fractionation did not affect, until five years and after five years, respectively: (1) local recurrence RR 0.90 (95% CI 0.68 to 1.18, P = 0.44) and RR 0.98 (95% CI 0.83 to 1.17, P = 0.86); (2) distant recurrence (RR) 1.04 (95% CI 0.73 to 1.46, P = 0.84) and RR 1.02 (95% CI 0.79 to 1.32, P = 0.88); (3) mortality RR 0.89 (95% CI 0.77 to 1.05, P = 0.16) and RR 0.96 (95% CI 0.89 to 1.08, P = 0.48); (4) disease-free survival RR 0.96 (95% CI 0.78 to 1.18, P = 0.69) and RR 0.96 (95% CI 0.84 to 1.09, P = 0.49); (5) cardiac ischemia RR 0.73 (95% CI 0.34 to 1.57, P = 0.42) and RR 0.61 (95% CI 0.33 to 1.15, P = 0.13); (6) rib fracture RR 1.02 (95% CI 0.25 to 4.20, P = 0.98) and RR 1.08 (95% CI 0.26 to 4.53, P = 0.91); (7) pulmonary fibrosis RR 2.42 (95% CI 0.50 to 11.71, P = 0.27) and RR 0.97 (95% CI 0.89 to 11.21, P = 0.07). **CONCLUSIONS:** Using hypofractioned radiotherapy regimens does not affect any of the outcomes analyzed in women with early stage breast cancer, after undergoing breast conservative surgery.

PCN5
RISK OF CARDIOTOXICITY AND ALL-CAUSE MORTALITY IN BREAST CANCER PATIENTS AFTER ADJUVANT CHEMOTHERAPY OR HORMONAL THERAPY
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OBJECTIVES: The purpose of this study was to estimate incidence of and identify factors associated with cardiotoxicity, defined as heart failure and/or cardiomyopathy, and all-cause mortality in breast cancer patients undergoing adjuvant chemotherapy or hormones. **METHODS:** A retrospective, population-based cohort study of 108,672 women (≥66 years of age) newly diagnosed with breast cancer from 2001-2009 was conducted using the Surveillance, Epidemiology, and End Results (SEER)-Medicare-linked database. Adjuvant chemotherapy were classified as mutually exclusive groups: trastuzumab-based, anthracycline-based, anthracycline and trastuzumab-based, taxane-based, and other chemotherapy. Propensity score matching adjusted for differences in patient characteristics across treatments. The final sample included a total of 11,250 women. Multivariable Cox proportional hazards regression models estimated hazard ratios (HRs) of cardiotoxicity and all-cause mortality with adjustment for inverse probability weights, sociodemographics, cancer characteristics, comorbidities, surgery and radiation, region, and year at diagnosis. **RESULTS:** Compared with hormones, risk of cardiotoxicity was higher in patients treated with anthracycline and trastuzumab-based (adjusted HR=1.87; 95% confidence intervals [CI]=1.51-2.33), trastuzumab-based (HR=1.32; 95%CI=1.14-1.52), and anthracycline-based (HR=1.14; 95%CI=1.03-1.27) regimens, respectively. Certain baseline characteristics were significant predictors of cardiotoxicity, including demographics (older age (vs. ≤70), non-Hispanic black), cancer characteristics (advanced stage), comorbidities (cardiovascular conditions or renal failure), year at diagnosis, and West region (vs. Northeast). Additionally, risk of all-cause mortality was higher in patients treated with taxane-based (HR=1.54; 95%CI=1.43-1.67) regimens compared to hormones. Baseline characteristics including sociodemographics, cancer characteristics, cardiovascular or renal failure comorbid conditions, year at diagnosis, and South region were significant predictors of all-cause mortality (all P<0.05). **CONCLUSIONS:** Women with breast cancer treated with trastuzumab-based and/or anthracycline-based regimens had increased cardiotoxicity risk compared with hormones, while those treated with taxane-based regimens had higher rates of all-cause mortality. Types of chemotherapy are associated with increased risk of cardiotoxicity and all-cause mortality. Practitioners should further evaluate treatment and patient characteristics for risk mitigation strategies.

PCN6
RACIAL/ETHNICITY DISPARITIES IN THE ASSOCIATION BETWEEN DIABETES AND PANCREATIC CANCER IN THE ELDERLY MEDICARE POPULATION
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OBJECTIVES: Although the relationship between diabetes and risk of pancreatic cancer are well-documented, limited research has examined whether racial/ethnicity differences accounted for the association between diabetes and pancreatic cancer. The aims of this study were to 1) assess whether diabetes is associated with pancreatic cancer in the elderly Medicare population, and 2) identify if any racial/